Remarks

Some informalities were pointed out in the Office Action mailed 8/4/08 (pp. 4-5). With respect to point 5 on p. 4, it is believed this resulted from a misreading of the claim and that the claim is in proper form. Other informalities have been corrected.

Claims 19-21 are objected to under 37 CFR 1.75(c) as allegedly not being of proper independent form and failing to further limit the subject matter of a previous claim (Office Action mailed 8/4/08, p. 5). This objection is respectfully traversed. Claim 1 recites a pharmaceutical composition containing specific constituents, and further requires that the composition increase the transmucosal absorption of the bioactive peptide constituent relative to its absorption in the absence of the cationic polyamino acid. Claims 19-21 further limit the claim in requiring that the increase in absorption be 2x, 5x and 10x, respectively, the absorption in the absence of the cationic polyamino acid. Therefore, claims 19-21 do indeed further limit claim 1 and are in proper dependent form. The MPEP passage cited in the Office Action mailed 8/4/08, p. 5, (MPEP 2111.04) refers to claim language that does not actually further limit the claim, such as "adapted to" or "adapted for," "wherein," or "whereby" clauses. But it also notes that the determination of whether each of these clauses is a limitation in a claim depends on the specific facts of the case, noting that in *Hoffer v. Microsoft Corp.*, 405 F.3d 1326, 1329, 74 USPQ2d 1481, 1483 (Fed. Cir. 2005), the court held that when a "'whereby' clause states a condition that is material to patentability, it cannot be ignored in order to change the substance of the invention." Here, it is a specific requirement of the dependent claim that the absorption is increased by the stated amount, and therefore is a genuine limitation of the claim that must be treated as any other. Reconsideration is respectfully requested.

Claim 1 stands rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Rothbard et al. (US 2002/0009491). This rejection is respectfully traversed.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be

shown in as complete detail as in contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). For anticipation, there must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the art. *Scripps Clinic & Res. Found. v. Genentech, Inc.*,, 18 USPQ2d 101 (Fed. Cir. 1991).

In the present case Rothbard does not disclose a composition where the bioactive peptide or protein of interest has the same net charge as the cationic polyamino acid at the pH of the composition. Rothbard explains at paragraph 44 that the components of the composition (delivery-enhancing transporters such as poly-Arg (paragraph 48), and the biologically active agent (paragraph 26)) "are held in an ionic association, typically viewed as an ion pair." Thus, these components necessarily have opposite net charges at the pH of the composition. Therefore, Rothbard does not anticipate the present claims.

Claims 1-4, 6-7, 9-10, 15-16, and 18-21 stand rejected under 35 U.S.C. 102(a) as allegedly being anticipated by Defelippis (WO 02/098348). Defelippis discloses a composition comprising particles where the particles are comprised of a GLP-1 compound complexed with a basic polypeptide, such as polylysine, polyarginine, polyornithine or others (p. 5, lines 1-6). But the present claims recite that the pharmaceutical composition has a pH at which the compatible buffer does not cause precipitation of the cationic polyamino acid. Defelippis discloses a composition at a pH where the polyamino acid is precipitated, since it is disclosed as being in particle form, whereas the present claims require that the buffer "does not cause precipitation of the cationic polyamio acid." Therefore, Defelippis does not anticipate the presently claimed invention.

Claims 1-10 and 15-26 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Young et al. (US 2003/0087820) in view of Baichwal (USP 5,330,761) and Ryser (USP 4,847,240). Young discloses a formulation comprising exendin, acetate buffer, mannitol as an iso-osmolality modifier (paragraphs 188-190 and 201). Young does not disclose a cationic polyamino acid at all, nor that the cationic polyamino acid has the same net charge as the

peptide or protein of interest. Young is also directed to providing exendins and agonists to the blood plasma (paragraph 12) through various means.

Baichwal discloses a tablet formulation containing an active ingredient that is not absorbed into the body but instead provides a localized effect (Col. 2, lines 33-37). The solid dosage form is bioadhesive when placed in contact with a mucous membrane (Col. 3, lines 21-24).

Ryser discloses that the cellular uptake of some molecules could be improved by the simple presence in the experimental medium of cationic polymers.

Ryser is not properly combinable with Young because combining Ryser with Young changes the principle of operation of Young. Young functions on a principle of introducing the bioactive peptide exendin into the blood plasma (paragraphs 11 and 12) through various means. But Ryser functions according to a principle of cellular uptake through diffusion or active transport (Col 1, line 26). The person of ordinary skill in the art finds no reason that a method of increasing active transport or diffusion into a cell would have any effect on increasing the concentration of a peptide in the bloodstream. Thus, the person of ordinary skill in the art would not combine the disclosure of Ryser, which is related to methods of increasing cellular uptake, with the disclosure of Young, which is related to methods of moving exendin into the bloodstream. Young and Ryser function according to different principles of operation. Modifying Young according to Ryser would therefore change the principle of operation of Young. MPEP 2143.01 VI. Ryser says nothing about how to introduce bioactive peptide into blood plasma or across mucosal membranes.

For the same reason modifying Young according to Ryser would render Young unsatisfactory for its intended purpose (MPEP 2143.01 V), which is to introduce exendin into blood plasma. For these reasons Young is not properly combinable with Baichwal and Ryser.

The present inventors discovered unexpectedly that the compositions of the invention act as transmucosal absorption enhancers for the bioactive peptide or protein. The present invention effectively delivers bioactive peptides and protein systematically to the blood subsequent to

transmucosal administration (specification, paragraph 18). None of the references, either alone or in combination, teach or suggest the presently claimed invention.

Claims 1-10 and 15-34 stand provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4-13, 18-26, 29-33, and 36-38 of copending Application No. 11/034,706. Application No. 11/034,706 is abandoned and therefore this rejection is inappropriate since no double patenting can occur with the cited Application.

Claims 1-10 and 15-34 stand provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3-12, 17-25, 28-32, 34-37, and 39-41 of copending Application No. 11/628,123. A terminal disclaimer is enclosed with this filing.

Closing

The Examiner is encouraged to call the undersigned to discuss any issues related to the prosecution of the instant application.

No fees are believed due with this Reply. However, if an additional fee is due, the Commissioner is hereby authorized to charge payment of any fees associated with this communication to applicant's **Deposit Account No. 010535**. Additionally, the Commissioner is hereby authorized to charge any underpayment or credit overpayment of fees during the pendency of this application to Applicant's **Deposit Account No. 010535**.

Respectfully submitted,

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